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CHILD RESISTANT BLISTER PACKAGES UTILIZING
WALLED STRUCTURES ENCLOSING MEDICAMENT THEREIN

Field and Background of the Invention

5 The invention generally relates to child resistant blister packages. The child-resistant ("CR") requirement for products packaged in blisters is typically dependent upon the toxicity level of any given product. Currently, the more toxic the drug, the more difficult the opening feature is made to gain access to the product in order to pass Consumer Product Safety Commission ("CPSC") protocol requirements. In
10 cases where a single tablet or capsule is considered harmful to a 25lbs. child, there are very few, if any, options available that are considered "user friendly". The existing options that pass official protocol testing require multiple steps that can be physically challenging and/or require an implement i.e.; scissors to open. Thus, there is a need in the art for a child-resistant blister package that addresses
15 problems associated with the above-mentioned existing options.

Summary of the Invention

 This invention substantially minimizes or prevents children from gaining access in accordance with the above protocol limits while at the same time is
20 capable of opening similarly to a non-CR push through blister design.

 More particularly, the invention provides a child resistant blister package. The child resistant blister package comprises a film having a surface wherein a plurality of cavities are formed therein containing at least one medicament; a cover sheet which overlies the cavities and is attached to the film;
25 and a wall structure raised above the surface of the film which extends throughout the film forming an interior region such that the plurality of cavities are enclosed within the interior region.

 Most children gain access to blister packaged products by biting through the clear blister material. In accordance with the present invention, the presence of the
30 wall structure substantially minimizes or eliminates the probability of a child from gaining access to a blister by penetrating the blister with his or her teeth.

Brief Description of the Drawings

FIG. 1 is a perspective view of a blister package in accordance with the present invention.

5 **FIG. 2** is a perspective view of a blister package in accordance with the present invention.

FIG. 3 is a side cross-sectional view of a blister package in accordance with the present invention.

FIG. 4 is a side cross-sectional view of a blister package in accordance with the present invention.

10 **FIG. 5** is a perspective view of a blister package in accordance with the present invention.

FIG. 6 is a perspective view of a blister package in accordance with the present invention.

15 **FIG. 7** is a perspective view of a blister package in accordance with the present invention.

FIG. 8 is a perspective view of a blister package in accordance with the present invention.

20 **FIG. 9** is a perspective view of a blister package in accordance with the present invention.

Detailed Description of the Embodiments

The present invention will now be described in reference to the embodiments set forth herein, including, without limitation, those described in the drawings. It should be appreciated that these embodiments are for illustrative purposes only, and are not intended to limit the scope of the invention as defined by the claims.

All publications, patents, and patent applications cited herein, whether *supra* or *infra*, are hereby incorporated herein by reference in their entirety to the same extent as if each individual publication, patent, or patent application was specifically and individually indicated to be incorporated by reference.

It must be noted that, as used in the specification and appended claims, the singular forms "a", "an" and "the" include plural referents unless the content clearly dictates otherwise.

In one aspect, the invention provides a child resistant blister package.

5 The child resistant blister package comprises a film having a surface wherein a plurality of cavities are formed therein containing at least one medicament; a cover sheet which overlies the cavities and is attached to the film; and a wall structure raised above the surface of the film which extends throughout the film forming an interior region such that the plurality of cavities are enclosed within the interior
10 region.

Various materials may be used in forming the film of the present invention. Examples materials include various materials formed from polymers that may include, without limitation, polyvinyl chloride, polyvinylidene chloride, polypropylene, polyethylene, polychlorotrifluoroethylene, and combinations thereof. The blisters
15 are formed by employing known techniques, such as application of vacuum.

The cover sheet may include various materials, non-limiting embodiments including cellulose, polymer, metal, as well as combinations thereof. In one embodiment, the cover sheet includes a metallic foil layer secured to the film and enclosing the opening of the blisters. The cover sheet is rupturable upon manual
20 compression of a blister containing medicament by a patient which releases the medicament. If employed, a metallic foil preferably comprises aluminum. In one embodiment, a first layer, formed from any of the materials set forth herein, is preferably backed by a second layer, preferably containing paperboard, such that the cover sheet is preferably present as a laminate. The cover sheet may be
25 attached to the film using a technique which is accepted in the art.

The blisters in the package of the invention may be present in numerous configurations. As an example, in one embodiment, the package may include at least one ordered arrangement (i.e., row or column) of blisters. In one embodiment, the package may include at least or two rows or columns of blisters.
30 In one embodiment, the package may include four rows or columns of blisters.

Examples of embodiments of materials employed in blister packages and methods of making the same are set forth in U.S. Patent Nos. 3,905,479;

3,912,082; 3,924,747; 3,835,995; 3,912,081; 3,924,746; 3,809,220; 3,809,221;
3,811,564; 3,872,970; 3,899,080; 3,921,805; and 3,941,248.

The term "medicament", as used herein, is meant to mean and include any substance (i.e., compound or composition of matter) which, when administered to
5 an organism (human or animal) induces a desired pharmacologic and/or physiologic effect by local and/or systemic action. The term therefore encompasses substances traditionally regarded as actives, drugs and bioactive agents, as well as biopharmaceuticals (e.g., peptides, hormones, nucleic acids, gene constructs, etc.) typically employed to treat a number of conditions which is defined broadly to
10 encompass diseases, disorders, infections, and the like. Exemplary medicaments include, without limitation, antibiotics, antivirals, H₂-receptor antagonists, 5HT₁ agonists, 5HT₃ antagonists, COX2-inhibitors, medicaments used in treating psychiatric conditions such as depression, anxiety, bipolar condition, tranquilizers, medicaments used in treating metabolic conditions, anticancer medicaments,
15 medicaments used in treating neurological conditions such as epilepsy and Parkinsons Disease, medicaments used in treating cardiovascular conditions, non-steroidal anti-inflammatory medicaments, medicaments used in treating Central Nervous System conditions, and medicaments employed in treating hepatitis.

Antivirals are particularly preferred. Examples of medicaments that are
20 effective for the treatment of viral and viral associated conditions are (1-alpha, 2-beta, 3-alpha)-9-[2,3-bis(hydroxymethyl)cyclobutyl]guanine [(-)BHCG, SQ-34514, lobucavir], 9-[(2R,3R,4S)-3,4-bis(hydroxymethyl)-2-oxetanosyl]adenine (oxetanocin-G), acyclic nucleosides, for example acyclovir, valaciclovir, famciclovir, ganciclovir, and penciclovir, acyclic nucleoside phosphonates, for example (S)-1-(3-hydroxy-2-
25 phosphonyl-methoxypropyl)cytosine (HPMPC), [[[2-(6-amino-9H-purin-9-yl)ethoxy]methyl]phosphinylidene]bis(oxymethylene)-2,2-dimethylpropanoic acid (bis-POM PMEA, adefovir dipivoxil), [[[1R)-2-(6-amino-9H-purin-9-yl)-1-methylethoxy]methyl]phosphonic acid (tenofovir), and (R)-[[2-(6-Amino-9H-purin-9-yl)-1-methylethoxy]methyl]phosphonic acid bis-(isopropoxy carbonyloxymethyl)ester
30 (bis-POC-PPMA), ribonucleotide reductase inhibitors, for example 2-acetylpyridine 5-[(2-chloroanilino)thiocarbonyl] thiocarbonohydrazide and hydroxyurea, nucleoside reverse transcriptase inhibitors, for example 3'-azido-3'-deoxythymidine

(AZT, zidovudine), 2',3'-dideoxycytidine (ddC, zalcitabine), 2',3'-dideoxyadenosine, 2',3'-dideoxyinosine (ddI, didanosine), 2',3'-didehydrothymidine (d4T, stavudine), (-)-beta-D-2,6-diaminopurine dioxolane (DAPD), 3'-azido-2',3'-dideoxythymidine-5'-H-phosphonate (phosphonovir), 2'-deoxy-5-iodo-uridine (idoxuridine), (-)-cis-1-(2-hydroxymethyl)-1,3-oxathiolane 5-yl)-cytosine (lamivudine), cis-1-(2-(hydroxymethyl)-1,3-oxathiolan-5-yl)-5-fluorocytosine (FTC), 3'-deoxy-3'-fluorothymidine, 5-chloro-2',3'-dideoxy-3'-fluorouridine, (-)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol (abacavir), 9-[4-hydroxy-2-(hydroxymethyl)but-1-yl]-guanine (H2G), ABT-606 (2HM-H2G) and ribavirin, protease inhibitors, for example indinavir, ritonavir, nelfinavir, amprenavir, saquinavir, (R)-N-tert-butyl-3-[(2S,3S)-2-hydroxy-3-N-[(R)-2-N-(isoquinolin-5-yloxyacetyl)amino-3-methylthio- propanoyl]amino-4-phenylbutanoyl]-5,5- dimethyl-1,3-thiazolidine-4-carboxamide (KNI-272), 4R-(4alpha,5alpha,6beta)-1,3-bis[(3-aminophenyl)methyl]hexahydro-5,6-dihydroxy-4,7-bis(phenylmethyl)-2H-1,3-diazepin-2-one dimethanesulfonate (mozenavir), 3-[1-[3-[2-(5-trifluoromethylpyridinyl)-sulfonylamino]phenyl]propyl]-4- hydroxy-6alpha-phenethyl-6beta-propyl-5,6-dihydro-2-pyranone (tipranavir), N'-[2(S)-Hydroxy-3(S)-[N-(methoxycarbonyl)-l-tert-leucylamino]-4- phenylbutyl-N^{alpha}-(methoxycarbonyl)-N'-[4-(2-pyridyl)benzyl]-L- tert-leucylhydrazide (BMS-232632), 3-(2(S)-Hydroxy-3(S)-(3-hydroxy-2-methylbenzamido)-4-phenylbutanoyl)-5,5-dimethyl-N-(2-methylbenzyl)thiazolidine-4(R)-carboxamide (AG-1776), N-(2(R)-hydroxy-1(S)-indanyl)-2(R)-phenyl-methyl-4(S)-hydroxy-5-(1-(1-(4-benzo[b]furanylmethyl)-2(S)-N'-(tert-butylcarboxamido)piperazinyl) pentanamide (MK-944A), and (3S)-tetrahydrofuran-3-yl (1S,2R)-[[[(4-aminophenyl)sulphonyl]] (isobutyl)amino]-1-benzyl-2-(phosphonoxy) propylcarbamate monocalcium salt (fosamprenavir), interferons such as α -interferon, renal excretion inhibitors such as probenecid, nucleoside transport inhibitors such as dipyrindamole; pentoxifylline, N-acetylcysteine (NAC), Procysteine, α -trichosanthin, phosphonoformic acid, as well as immunomodulators such as interleukin II or thymosin, granulocyte macrophage colony stimulating factors, erythropoetin, soluble CD₄ and genetically engineered derivatives thereof, non-nucleoside reverse transcriptase inhibitors (NNRTIs), for example nevirapine (BI-RG-587), alpha-((2-acetyl-5-methylphenyl)amino)-2,6-dichloro-

benzeneacetamide (loviride), 1-[3-(isopropylamino)-2-pyridyl]-4-[5-(methanesulfonamido)-1H-indol-2-ylcarbonyl]piperazine monomethanesulfonate (delavirdine), (10R, 11S, 12S)-12-Hydroxy-6, 6, 10, 11-tetramethyl-4-propyl-11,12-dihydro-2H, 6H, 10H-benzo(1, 2-b:3, 4-b':5, 6-b'')tripyrans-2-one ((+) calanolide A),
5 (4S)-6-Chloro-4-[1E)-cyclopropylethenyl]-3,4-dihydro-4-(trifluoromethyl)-2(1H)-quinazolinone (DPC-083), (S)-6-chloro-4-(cyclopropylethynyl)-1,4-dihydro-4-(trifluoromethyl)-2H-3,1-benzoxazin-2-one (efavirenz, DMP 266), 1-(ethoxymethyl)-5-(1-methylethyl)-6-(phenylmethyl)-2,4(1H,3H)-pyrimidinedione (MKC-442), and 5-(3,5-dichlorophenyl)thio-4-isopropyl-1-(4-pyridyl)methyl-1H-imidazol-2-ylmethyl
10 carbamate (capravirine), glycoprotein 120 antagonists, for example PRO-2000, PRO-542 and 1,4-bis[3-[(2, 4-dichlorophenyl)carbonylamino]-2-oxo-5,8-disodiumsulfanyl]naphthalyl-2, 5-dimethoxyphenyl-1, 4-dihydrazone (FP-21399), cytokine antagonists, for example reticulose (Product-R), 1,1'-azobis-formamide (ADA), 1,11-(1,4-phenylenebis(methylene))bis-1,4,8,11-tetraazacyclotetradecane
15 octahydrochloride (AMD-3100), integrase inhibitors, for example, S-1360, and fusion inhibitors.

The term medicament also encompasses pharmaceutically acceptable salts, esters, solvates, and/or hydrates of the pharmaceutically active substances referred to hereinabove. Various combinations of any of the above medicaments may also
20 be employed.

In accordance with the present invention, the medicament is typically employed in an oral pharmaceutical formulation. An oral pharmaceutical formulation typically refers to the combination of at least one medicament and one or more added components or elements, such as an "excipient" or "carrier." As will
25 be appreciated by one having ordinary skill in the art, the terms "excipient" and "carrier" generally refer to substantially inert materials that are nontoxic and do not interact with other components of the composition in a deleterious manner. Examples of normally employed "excipients," include pharmaceutical grades of carbohydrates, including monosaccharides, disaccharides, cyclodextrins and
30 polysaccharides (e.g., dextrose, sucrose, lactose, raffinose, mannitol, sorbitol, inositol, dextrans and maltodextrins); starch; cellulose; salts (e.g., sodium or calcium phosphates, calcium sulfate, magnesium sulfate); citric acid; tartaric acid; glycine;

leucine; high molecular weight polyethylene glycols (PEG); pluronics; surfactants; lubricants; stearates and their salts or esters (e.g., magnesium stearate); amino acids; fatty acids; and combinations thereof.

5 The oral pharmaceutical formulation may be utilized in a variety of unit dosage forms including, without limitation, a tablet, a pill, a capsule, a lozenge, and combinations thereof. The unit dosage forms may encompass hospital unit dosage forms, as well as others.

10 In one embodiment, a combination of lamivudine, zidovudine, and nevirapine is employed in the blister package. More specifically, it is preferred to employ the above medicaments in a combination regimen wherein a first pharmaceutical formulation includes lamivudine and zidovudine and a second pharmaceutical formulation include nevirapine. In such an embodiment, it is preferred that the first pharmaceutical formulation and the second pharmaceutical formulation be present in unit dosage forms in discrete blisters.

15 The invention will now be described with respect to the drawings. It should be appreciated that the drawings are merely set forth to illustrate the invention and do not serve to limit the scope of the invention as defined by the claims.

FIGS. 1-7 illustrate blister packages **10** in accordance with the present invention. As shown, the package **10** includes a film **20** having a surface **30** and plurality of cavities or blisters **40** formed therein. The cavities **40** are configured to house at least one medicament in unit dosage form. A cover sheet **50** is present on the bottom of film **20** and is bonded thereto. Film **20** preferably has a thickness ranging from about 0.7 mm to about 2.0 mm. As shown, the cover sheet **50** overlies cavities **40**. As stated herein, the cover sheet **50** may include a plurality of layers as described herein and can be present in the form of a laminate. The cover sheet **50** preferably has a thickness ranging from about 0.025 mm to about 0.076 mm.

30 As shown, a wall structure **60** is present which is above the film surface **30**. In particular, the wall structure **60** is coextensive with the periphery or outer edge of the film **20** (preferably extending parallel or substantially parallel to the film periphery) forming an interior region **25** within the film **20** so as to enclose the

cavities **40** therein. As shown, the wall structure **60** rises from the film surface having a first face extending from the film surface proximal to the outer film edge **70** and a second face extending from the film surface distal to the outer film edge **70**. A top portion may additionally be present to adjoin the two faces. The wall structure **60** is configured so as to leave a certain surface area (denoted as **s**) of film between it and the cavities **40**. The wall structure **60** may be unitary with the film **20** or may be employed as a separate structure which is positioned on the film **20**. Preferably, the wall structure **60** can be formed from a number of materials such as, without limitation, polyvinyl chloride, polyvinylidene chloride, polypropylene, polyethylene, polychlorotrifluoroethylene, as well as combinations thereof. The wall structure **60** may be transparent or opaque. Advantageously, the wall structure **60** is dimensioned and positioned such that the probability of a child accessing medicament in a blister is substantially reduced or eliminated. Preferably, the distance from the outer edge **70** of the blister pack **10** to the edge of wall structure **60** proximal to outer edge **70** (denoted as **d₁**) ranges from about 3.175 mm to about 25.4 mm. Preferably, the top height of the wall structure **60** (denoted as **h₁**) ranges from about 3.175 mm to about 12.7 mm. Preferably, the distance from a row or column of cavities **40** to the edge of the wall structure **60** proximal to the row or column of cavities (denoted as **d₂**) ranges from about 3.175 mm to about 12.7 mm.

A cross-sectional side view of the blister pack **10** is illustrated in **FIGS. 3-4**. In particular, **FIG. 3** illustrates an end view of blister pack **10** and **FIG. 4** illustrates a view of blister pack **10** along its length. Referring to **FIG. 4**, wall structure **60** may be solid or have void spaces present therein, and includes a face **61** proximal to outer edge **70** and a face **62** distal to outer edge **70**. Faces **61** and **62** are connected via top portion **65** in this embodiment. As seen in these embodiments, the wall structure **60** has a largely triangular cross-section. Nonetheless, it should be appreciated by one skilled in the art that the wall structure may encompass other geometries without departing from the scope of the invention. For example, the cross-section of the wall structure may be rectangular as denoted by dashed lines in **FIGS. 3-4**. Moreover, it should be appreciated that the structure may have rounded corners as well as those which are present as illustrated in **FIGS. 3-4** denoted as

65. Notwithstanding the geometry of the wall structure **60** illustrated in **FIGS. 3-4**, the wall structure **60** preferably has a width (denoted as d_3) ranging from about 3.175 mm to about 12.7 mm. Preferably, the distance from the top of a blister to the top of the wall structure (denoted as d_4) ranges from about 0 mm to about 6.35 mm.

As shown in **FIGS. 2, 5 and 6**, the blister package **10** may encompass multiple columns. Such packages may be fabricated according to techniques known in the art. As an example, the structure of the blister columns may be separately assembled and thereafter joined together by using, for example, ultrasonic welding.

The blister package **10** according to the present invention may be employed in a variety of capacities. As an example, the blister package **10** can be used as a sample package, i.e., a package which may include, in various non-limiting embodiments, a one-day or two week supply of medicament. Additionally, the blister package **10** may be employed as a compliance package, i.e., a package used for assisting the patient in conforming with his or her prescribed dosage regimen. Embodiments of compliance packages are set forth in **FIGS. 5 and 7**. As illustrated, in this embodiment, labels **A.M.** and **P.M.** are assigned to the top of each column designating the time of day for taking the medicament corresponding to each row. Although not explicitly indicated, each row in these embodiments corresponds to a single day.

In non-limiting examples as shown in **FIGS. 6-7**, a wall structure **60'** may be present between two blister columns so as to separate the columns and provide further protection against a child potentially gaining access to medicament.

FIG. 8 depicts a blister package **10** having four columns and seven rows. Such a blister package **10** can be used in a variety of manners. As an example, in one non-limiting embodiment, the two columns on the far left may contain two distinct pharmaceutical formulations present in discrete blisters, i.e., one column contains a first pharmaceutical formulation and the second column contains a second pharmaceutical formulation. Likewise, the third column from left may contain the first pharmaceutical formulation and the fourth column from left contains

the second pharmaceutical formulation. In such an embodiment, the first and second columns represent the A.M. dosages and the third and fourth columns represent the P.M. dosages. It should be appreciated that a number of deviations from this embodiment can be made. For example, all four columns may all contain
5 distinct formulations or the same or similar formulations.

FIG. 9 illustrates an embodiment of a blister package **10** in accordance with the present invention. As shown, blister package **10** has a plurality of columns present on various flats (denoted as **80**, **90**, **100**, and **110**). The flats are joined by hinges **120**, **130**, and **140** such that the flats may fold into an convenient overlapped
10 structure. Tongue **150** is configured to fit in slot **160** to secure package **10**.

Notwithstanding the embodiments set forth in the figures herein, it should be appreciated that any number of rows and/or columns may be employed in the blister package of the present invention in addition to these embodiments.

The present invention has been described with respect to the embodiments
15 set forth herein. Nonetheless, it should be noted that such embodiments are merely set forth to illustrate the invention, and do not limit its scope as defined by the claims set forth herein.